Arianna Fumagalli
Medical Oncology Department - Integrated University Hospital of Verona (Italy)
ENETS Center of Excellence

Syndromic shift of a non-functioning pancreatic NEN

DISCLOSURE OF INTEREST

- None

Syndromic shift of a non functioning pancreatic NEN

Male, 63 years old, ECOG = 0. Medical history: previous necrotic-hemorrhagic pancreatitis (2016). Symptoms: abdominal pain.

- Abdominal US and Thoraco-abdominal CT (April 2017): **Cephalopancreatic lesion (7x6cm) associated with diffuse hepatic metastasis and lymph nodes involvement** (**pT3N1M1**)
- CgA 1269 ng/ml, NSE 32,6 µg/l
- Transabdominal pancreatic biopsy: **Well-differentiated pancreatic neuroendocrine tumor, Ki67 30% (NET G3)**
- Double tracer ^{68}Ga-DOTATOC and ^{18}FDG PET/CT: heterogeneous receptor uptake → high expression on nodal metastasis and primary (SUV max 41) low/no expression on liver metastasis (SUV max 15). Moderate hypermetabolism on all known lesions
- May-November 2017: Chemotherapy (CDDP-DTIC-5FU, 6 cycles) with SD as best OR according to RECIST criteria

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January 2018: hospitalization for **persistent hypokalemia (about 2 mmol/l), uncontrolled diabetes and arterial hypertension.** Severe signs/symptoms suspected for Cushing syndrome.

No clinical benefit with continuous ev infusion of potassium (up to 200 mEq/day)

- Plasmatic cortisol levels > 2000 nmol/l (range 120-620)
- Urinary cortisol levels/24 hours 12375 nmol
- ACTH levels at 8:00 am 54.2 pmol/l and at 8:00 pm 60.2 pmol/l
- DHEA 6.97 µmol/l

Exclusion of other causes of ACTH hypersecretion.

Clinical diagnosis : **Severe Cushing Syndrome due to ACTH ectopic secretion**

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Treated with **ketoconazole** and **octreotide analogues** with early normalization of potassium and plasmatic cortisol levels (534 nmol/l).

Rapid worsening of cortisol (1013 nmol/l) and ACTH (67.4 pmol/l): **metyrapone** was added to ketoconazole with clear clinical benefit.

- Thoraco-abdominal CT scan (January 2018): SD, increased dimension of adrenal glands, widespread osteopenia.
- 68Ga-DOTATOC PET/CT (January 2018): increase in receptor uptake in liver lesions; stability in other known sites.

Multidisciplinary discussion: proposed **unilateral adrenalectomy** (in order to lower amount of drugs needed to correct hypercortisolism) and subsequent **PRRT treatment after PD**.

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Discussion

- Severe **ectopic ACTH secretion** is a challenging clinical scenario that requires **prompt diagnosis and treatment**;
- Syndromic shift of a non-functioning neuroendocrine tumor is an **uncommon event** usually associated with **worse prognosis**;
- High ACTH/cortisol levels can affect **somatostatin receptors expression**;
- Drugs required to correct ectopic ACTH syndrome can interfere with antitumor drugs;
- **"Palliative surgery"** is an option for functioning tumours even in the case of high tumor burden;
- **Multidisciplinary discussion** is essential due the complexity of this pathology.